

*Preliminary Amendment*

*Serial No. 09/937,076*

*Confirmation No. 4527*

METHODS OF USE OF  $\beta$ 1-INTEGRIN INHIBITORS

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**Amendments to the Claims**

This listing of claims replaces all prior versions, and listings, of claims in the above-identified application:

1. (currently amended) A method of inhibiting inflammatory leukocyte mediated destruction of tissue in a patient, the method comprising administering to the patient a composition comprising a  $\beta$ 1-integrin inhibitor having the amino acid sequence OPPRAAIY (SEQ ID NO:3).
2. (cancel) The method of claim 1 wherein the  $\beta$ 1-integrin inhibitor is a peptide comprising a C-terminal LipAr motif.
3. (cancel) The method of claim 2 wherein the  $\beta$ 1-integrin inhibitor is a peptide comprising an amino acid sequence selected from the group consisting of WQPPRARIY (SEQ ID NO:1), WQPPRAAIY (SEQ ID NO:2), QPPRAAIY (SEQ ID NO:3), WQPPAARIY (SEQ ID NO:4), AQPPRARIY (SEQ ID NO:5), WAPPRARIY (SEQ ID NO:6), WQPPDADIY (SEQ ID NO:7), ARITGYIY (SEQ ID NO:8), RARITGYIY (SEQ ID NO:9), PRQAWRPIY (SEQ ID NO:10), RPAPQRWIY (SEQ ID NO:11), PRARIY (SEQ ID NO:12), RARIY (SEQ ID NO:13), ARIY (SEQ ID NO:14), and RIY.
4. (original) The method of claim 1 wherein the composition further includes a pharmaceutically acceptable carrier.
5. (original) The method of claim 1 wherein the inflammatory leukocyte mediated destruction of tissue occurs as a result of CNS ischemic injury, myocardial infarction, angioplasty, surgical incisions, injury-related trauma, transplant reperfusion, or a combination thereof.

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6. (original) The method of claim 1 wherein the inflammatory leukocyte mediated destruction of tissue occurs as a result of exposure to heat, cold, light, electricity, chemicals, or a combination thereof.
7. (currently amended) A method of treating a stroke patient, the method comprising administering to the patient a composition comprising a  $\beta$ 1-integrin inhibitor having the amino acid sequence QPPRAAIY (SEQ ID NO:3) in an amount effective to reduce infarct size, reduce neurological deficit, or both.
8. (original) The method of claim 7 wherein the composition is administered locally.
9. (original) The method of claim 8 wherein the  $\beta$ 1-integrin inhibitor is administered in an amount effective to reduce the infarct size by at least about 80%.
10. (original) The method of claim 8 wherein the  $\beta$ 1-integrin inhibitor is administered in an amount effective to reduce the neurological deficits by at least about 80%.
11. (canceled) The method of claim 7 wherein the  $\beta$ 1-integrin inhibitor is a peptide comprising a C-terminal LipAr motif.
12. (canceled) The method of claim 11 wherein the  $\beta$ 1-integrin inhibitor is a peptide comprising an amino acid sequence selected from the group consisting of WQPPRARIY (SEQ ID NO:1), WQPPRAAIY (SEQ ID NO:2), QPPRAAIY (SEQ ID NO:3), WQPPAARIY (SEQ ID NO:4), AQPPRARIY (SEQ ID NO:5), WAPPRARIY (SEQ ID NO:6), WQPPDADIY (SEQ ID NO:7), ARITGYIY (SEQ ID NO:8), RARITGYIY (SEQ ID NO:9), PRQAWRPIY (SEQ ID NO:10), RPAPQRWIY (SEQ ID NO:11), PRARIY (SEQ ID NO:12), RARIY (SEQ ID NO:13), ARIY (SEQ ID NO:14), and RIY.

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13. (currently amended) A method of treating a patient having a burn-type injury, the method comprising administering a composition comprising a  $\beta$ 1-integrin inhibitor having the amino acid sequence OPPRAAIY (SEQ ID NO:3) in an amount effective and over a period of time effective to reduce leukocyte-mediated tissue destruction.
14. (canceled) The method of claim 13 wherein the  $\beta$ 1-integrin inhibitor is a peptide comprising a C-terminal LipAr motif.
15. (canceled) The method of claim 14 wherein the  $\beta$ 1-integrin inhibitor is a peptide comprising an amino acid sequence selected from the group consisting of WQPPRARIY (SEQ ID NO:1), WQPPRAAIY (SEQ ID NO:2), QPPRAAIY (SEQ ID NO:3), WQPPAARIY (SEQ ID NO:4), AQPPRARIY (SEQ ID NO:5), WAPPRARIY (SEQ ID NO:6), WQPPDADIY (SEQ ID NO:7), ARITGYIY (SEQ ID NO:8), RARITGYTY (SEQ ID NO:9), PRQAWRPIY (SEQ ID NO:10), RPAPQRWIY (SEQ ID NO:11), PRARIY (SEQ ID NO:12), RARIY (SEQ ID NO:13), ARIY (SEQ ID NO:14), and RIY.
16. (canceled) The method of claim 15 wherein the  $\beta$ 1-integrin inhibitor is a peptide comprising the amino acid sequence WQPPRARIY (SEQ ID NO:1).
17. (original) The method of claim 13 wherein the period of time is at least 1 hour.
18. (original) The method of claim 17 wherein the period of time is at least 24 hours.
19. (original) The method of claim 18 wherein the period of time is at least 48 hours.
20. (original) The method of claim 13 wherein the composition is administered periodically over a predetermined period of time.

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21. (currently amended) A method of treating a burn patient, the method comprising maintaining a composition comprising an effective amount of a  $\beta$ 1-integrin inhibitor having the amino acid sequence OPPRAAIY (SEQ ID NO:3) on a burn-type injury for a period of time effective to reduce leukocyte-mediated tissue destruction and achieve a desired degree of healing.
22. (canceled) The method of claim 21 wherein the  $\beta$ 1-integrin inhibitor is a peptide comprising a C-terminal LipAr motif.
23. (canceled) The method of claim 22 wherein the  $\beta$ 1-integrin inhibitor is a peptide comprising an amino acid sequence selected from the group consisting of WQPPRARIY (SEQ ID NO:1), WQPPRAAIY (SEQ ID NO:2), QPPRAAIY (SEQ ID NO:3), WQPPAARIY (SEQ ID NO:4), AQPPRARIY (SEQ ID NO:5), WAPPRARIY (SEQ ID NO:6), WQPPDADIY (SEQ ID NO:7), ARITGYIY (SEQ ID NO:8), RARITGYIY (SEQ ID NO:9), PRQAWRPIY (SEQ ID NO:10), RPAPQRWIY (SEQ ID NO:11), PRARIY (SEQ ID NO:12), RARIY (SEQ ID NO:13), ARIY (SEQ ID NO:14), and RIY.
24. (canceled) The method of claim 23 wherein the  $\beta$ 1-integrin inhibitor is a peptide comprising the amino acid sequence WQPPRARIY (SEQ ID NO:1).
25. (currently amended) A method of treating a cancer patient, the method comprising administering to the patient a composition comprising a  $\beta$ 1-integrin inhibitor having the amino acid sequence OPPRAAIY (SEQ ID NO:3) in an amount effective to inhibit one or more of angiogenesis, cancer cell metastasis, cancer cell motility, or cancer cell migration.
26. (canceled) The method of claim 25 wherein the  $\beta$ 1-integrin inhibitor is a peptide comprising a C-terminal LipAr motif.

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27. (canceled) The method of claim 26 wherein the  $\beta$ 1-integrin inhibitor is a peptide comprising an amino acid sequence selected from the group consisting of WQPPRARIY (SEQ ID NO:1), WQPPRAAIY (SEQ ID NO:2), QPPRAAIY (SEQ ID NO:3), WQPPAARIY (SEQ ID NO:4), AQPPRARIY (SEQ ID NO:5), WAPPRARIY (SEQ ID NO:6), WQPPDADIY (SEQ ID NO:7), ARITGYIY (SEQ ID NO:8), RARITGYIY (SEQ ID NO:9), PRQAWRPIY (SEQ ID NO:10), RPAPQRWIY (SEQ ID NO:11), PRARIY (SEQ ID NO:12), RARIY (SEQ ID NO:13), ARIY (SEQ ID NO:14), and RIY.

28. (currently amended) A method of treating a cancer patient, the method comprising administering to the patient a composition comprising a  $\beta$ 1-integrin inhibitor having the amino acid sequence QPPRAAIY (SEQ ID NO:3) in an amount effective to induce programmed cell death in cancerous tissue or restore normal cellular phenotype to cancerous tissue.

29. (canceled) The method of claim 28 wherein the  $\beta$ 1-integrin inhibitor is a peptide comprising a C-terminal LipAr motif.

30. (canceled) The method of claim 29 wherein the  $\beta$ 1-integrin inhibitor is a peptide comprising an amino acid sequence selected from the group consisting of WQPPRARIY (SEQ ID NO:1), WQPPRAAIY (SEQ ID NO:2), QPPRAAIY (SEQ ID NO:3), WQPPAARIY (SEQ ID NO:4), AQPPRARIY (SEQ ID NO:5), WAPPRARIY (SEQ ID NO:6), WQPPDADIY (SEQ ID NO:7), ARITGYIY (SEQ ID NO:8), RARITGYIY (SEQ ID NO:9), PRQAWRPIY (SEQ ID NO:10), RPAPQRWIY (SEQ ID NO:11), PRARIY (SEQ ID NO:12), RARIY (SEQ ID NO:13), ARIY (SEQ ID NO:14), and RIY.

31. (original) The method of claim 28 further comprising administering a compound that inhibits the enzymatic degradation of the  $\beta$ 1-integrin inhibitor.

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32. (currently amended) A method of treating a patient for osteoporosis, the method comprising administering to the patient a composition comprising a  $\beta$ 1-integrin inhibitor having the amino acid sequence OPPRAAIY (SEQ ID NO:3) in an amount effective to inhibit osteoclast adhesion and bone resorption.

33. (canceled) The method of claim 32 wherein the  $\beta$ 1-integrin inhibitor is a peptide comprising a C-terminal LipAr motif.

34. (canceled) The method of claim 33 wherein the  $\beta$ 1-integrin inhibitor is a peptide comprising an amino acid sequence selected from the group consisting of WQPPRARIY (SEQ ID NO:1), WQPPRAAIY (SEQ ID NO:2), QPPRAAJY (SEQ ID NO:3), WQPPAARIY (SEQ ID NO:4), AQPPRARIY (SEQ ID NO:5), WAPPRARIY (SEQ ID NO:6), WQPPDADIY (SEQ ID NO:7), ARITGYIYY (SEQ ID NO:8), RARITGYIY (SEQ ID NO:9), PRQAWRPIY (SEQ ID NO:10), RPAPQRWIY (SEQ ID NO:11), PRARIY (SEQ ID NO:12), RARIY (SEQ ID NO:13), ARIY (SEQ ID NO:14), and RIY.

35. (currently amended) A method of peripheralizing stem cells, the method comprising administering to a patient a composition comprising a  $\beta$ 1-integrin inhibitor having the amino acid sequence OPPRAAIY (SEQ ID NO:3).

36. (canceled) The method of claim 35 wherein the  $\beta$ 1-integrin inhibitor is a peptide comprising a C-terminal LipAr motif.

37. (canceled) The method of claim 36 wherein the  $\beta$ 1-integrin inhibitor is a peptide comprising an amino acid sequence selected from the group consisting of WQPPRARIY (SEQ ID NO:1), WQPPRAAIY (SEQ ID NO:2), QPPRAAIY (SEQ ID NO:3), WQPPAARIY (SEQ ID NO:4), AQPPRARIY (SEQ ID NO:5), WAPPRARIY (SEQ ID NO:6), WQPPDADIY (SEQ ID NO:7), ARITGYIYY (SEQ ID NO:8), RARITGYIY (SEQ ID NO:9), PRQAWRPIY (SEQ ID NO:10), RPAPQRWIY (SEQ ID NO:11), PRARIY (SEQ ID NO:12), RARIY (SEQ ID NO:13), ARIY (SEQ ID NO:14), and RIY.

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NO:10), RPAPQRWIY (SEQ ID NO:11), PRARIY (SEQ ID NO:12), RARIY (SEQ ID NO:13), ARIY (SEQ ID NO:14), and RIY.

38. (currently amended) A composition comprising  $\beta$ 1-integrin inhibitor having the amino acid sequence OPPRAAIY (SEQ ID NO:3) and a pharmaceutically acceptable carrier.

39. (canceled) The composition of claim 38 wherein the  $\beta$ 1-integrin inhibitor is a peptide comprising a C-terminal LipAr motif.

40. (canceled) The composition of claim 39 wherein the  $\beta$ 1-integrin inhibitor is a peptide comprising an amino acid sequence selected from the group consisting of WQPPRARIY (SEQ ID NO:1), WQPPRAAIY (SEQ ID NO:2), QPPRAAIY (SEQ ID NO:3), WQPPAARIY (SEQ ID NO:4), AQPPRARIY (SEQ ID NO:5), WAPPRARIY (SEQ ID NO:6), WQPPDADIY (SEQ ID NO:7), ARITGYIYY (SEQ ID NO:8), RARITGYIYY (SEQ ID NO:9), PRQAWRPIY (SEQ ID NO:10), RPAPQRWIY (SEQ ID NO:11), PRARIY (SEQ ID NO:12), RARIY (SEQ ID NO:13), ARIY (SEQ ID NO:14), and RIY.